

Trends in gonococcal resistance to antibiotics in Rotterdam, the Netherlands, 1975-86

J H T WAGENVOORT,* J H VAN RIJSOORT-VOS,* J A J W KLUIJTMANS,*
M J KIESKAMP,* E STOLZ,† M F MICHEL,*

From the departments of *Clinical Microbiology and †Dermatovenereology, University Hospital Dijkzigt, Rotterdam, the Netherlands

SUMMARY The incidence of resistance of *Neisseria gonorrhoeae* to penicillin and tetracycline was periodically monitored during 1975-86. The incidence of resistance to penicillin (minimum inhibitory concentration (MIC) of more than 1.28 mg/l) of non-PPNG strains remained low (less than 2.5%). The incidence of penicillinase producing *N gonorrhoeae* (PPNG) strains decreased after a peak of 14% in 1982 to a mean of 8% in more recent years. After a gradual increase, the incidence of tetracycline resistant (MIC of more than 1.28 mg/l) strains has remained stable at around 20% during the past five years. This indicates that a continuing increase in incidence of resistance was not observed in this outpatient clinic.

Past decades have shown an increasing incidence of resistance of *Neisseria gonorrhoeae* to antibiotics. This included the emergence of penicillinase producing *N gonorrhoeae* (PPNG) strains as well as chromosomally or plasmid mediated resistance to penicillin and tetracycline.¹⁻³ The trend of changing patterns of resistance prompted us to monitor its development. Since 1975 we have periodically surveyed the sensitivity to penicillin and tetracycline of *N gonorrhoeae* strains obtained from patients attending the outpatient clinic of venereology.

We report here our findings regarding the in vitro sensitivity of these strains of *N gonorrhoeae*.

Patients, materials, and methods

We cultured strains of *N gonorrhoeae* from patients (civilians and sailors) attending the venereology outpatient clinic of this hospital. These strains were isolated and identified according to standard procedures.⁴

For this investigation we collected consecutively isolated but independent *N gonorrhoeae* strains for two months at the beginning of each year from 1975

to 1986. The number of strains tested in each two month period varied from 139 to 273. Minimum inhibitory concentrations (MICs) of penicillin and tetracycline were measured by the standard agar dilution method on a gonococcal agar medium, as described previously.⁴ Assays were performed with a bacterial inoculum of 10⁴ colony forming units (cfu) per spot, using twofold dilutions of antibiotics ranging between 5.12 mg/l and 0.005 mg/l. The strains were classified as being sensitive or resistant according to their MICs. Resistance was defined by an MIC of more than 1.28 mg/l. All strains were tested for β lactamase production by the chromogenic cephalosporin test (Nitrocephin) to detect PPNG strains.

Results

The table shows the sensitivity pattern of the *N gonorrhoeae* strains isolated during the periods monitored. The percentage of non-PPNG strains with MICs of penicillin of more than 1.28 mg/l was less than 2.5% and did not alter appreciably during these years. The percentage of strains with MICs of tetracycline of more than 1.28 mg/l increased substantially from less than 3% in 1975-79 to 36% in 1982. The mean percentage in 1982-86 was 21%.

The percentages of PPNG strains increased from 2% in 1976⁵ to a maximum of 14% in 1982. After 1982 the mean percentage decreased to 8%. The mean percentage in the period 1979-86 was 7%.

Address for reprints: Dr JHT Wagenvoort, Department of Clinical Microbiology, University Hospital Dijkzigt, Dr Molewaterplein 40, 3015 GD Rotterdam, the Netherlands

Table Range of resistance* of *Neisseria gonorrhoeae* to penicillin and tetracycline in Rotterdam, first two months of 1975–86

Year	No	No (%) non-PPNG strains resistant* to:		No (%) PPNG strains
		Penicillin	Tetracycline	
1975	242	3 (1.2)	7 (2.9)	0
1976	139	0	4 (2.9)	0
1977	262	1 (0.4)	4 (1.5)	0
1978	270	Not tested	Not tested	0
1979	254	1 (0.4)	2 (0.8)	5 (2.0)
1980	258	3 (1.2)	9 (3.5)	6 (2.3)
1981	273	4 (1.5)	14 (5.1)	24 (8.8)
1982	253	5 (2.0)	90 (35.6)	35 (13.8)
1983	269	4 (1.5)	50 (18.6)	32 (11.9)
1984	257	5 (2.0)	52 (20.2)	12 (4.7)
1985	270	2 (0.7)	50 (18.5)	20 (7.4)
1986	246	6 (2.4)	29 (11.8)	17 (6.9)

*Resistance defined by minimum inhibitory concentration of > 1.28 mg/l.

in 1981–82. Thereafter, incidence stabilised at a much higher level than before. High level resistance (MICs of 16–32 mg/l) of *N gonorrhoeae* to tetracycline was first reported in 1985.⁷ Screening for this level of resistance of the strains tested in 1986 proved negative. Moreover, measurement of MICs of tetracycline against more than 500 other *N gonorrhoeae* strains, performed during studies of antigenococcal treatment with antibiotics,⁹ showed maximum MICs of tetracycline of 4 mg/l.

We conclude that stabilisation, rather than an increase in the incidence of resistant strains, has been observed in our institute in the past four years. Despite these findings, continued monitoring would seem to be justified to detect any sudden emergence of new forms or changing patterns of incidence of resistance.

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Discussion

Chromosomally mediated resistance of *N gonorrhoeae* strains is generally defined by an MIC of penicillin of more than 1 mg/l.^{3,6} This MIC is also considered to define resistance to tetracycline.^{6,7} Such MICs correlate with increased treatment failure rates with these drugs.⁸ We chose the nearest MIC (1.28 mg/l) as the break point to define resistance. All PPNG strains were regarded as being resistant to penicillin.

PPNG strains were first isolated in this outpatient clinic in 1976,⁵ outside the two month period monitored here. The yearly numbers of infections with PPNG strains in 1976, 1977, and 1978 were 3, 4, and 6 respectively, which contributed less than 0.5% to the total number of strains isolated in these years. This observation indicates that the results of the periods monitored may not always completely reflect the yearly pattern. The percentage of PPNG strains fell from its zenith in 1982 to an average of 7.8% from 1983 onwards. This trend was also observed in Great Britain.³

The incidence of penicillin resistant non-PPNG strains remained low (0–2.4%) without substantial changes during the study. For tetracycline, however, a sudden unexplained increase in resistance was noted

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